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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/809,677	02/20/2002	Edward F. Myers	07354/004001	7900

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James W McClain
Brown Martin Haller & McClain
1660 Union Street
San Diego, CA 92101

EXAMINER	
KIM, SUN U	

ART UNIT	PAPER NUMBER
1723	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/809,677	MYERS, EDWARD F.	
	Examiner	Art Unit	
	John Kim	1723	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27 and 29-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27 and 30-43* is/are rejected.

7)☒ Claim(s) *29 and 44-46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Claims 1-16, 41-42 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-15 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: a metal containing substrate and the rest of the structural elements. Claim 1 is indefinite for failing to demonstrate whether a metal containing substrate is provided outside the device or in a location such as a mixing vessel. Recitation of "the biological reactor" on line 8 of claim 16 lacks a positive antecedent basis. Claims 16 and 41 are indefinite for failing to particularly point out whether hepatocytes circulated are hepatocytes attached to a metal containing substrate. Claim 42 is indefinite for failing to further limit the scope of independent claim 41 in that hepatocytes are allowed to attach to a metal containing substrate.

2. Claims 1-2, 7-8, 12, 14-21, 24-27, 32, 35, 37-38 and 41-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olumide et al., "Hepatic support with hepatocyte suspensions in a permeable membrane dialyzer", Surgery, November 1977, Vol. 82, No. 5, pages 599-606 (hereinafter referred to as Olumide et al.) in view of U.S. Patent No. 4,963,490 (hereinafter referred to as Churchouse et al). Olumide et al. teach method and apparatus for extracorporeal purification of blood and plasma comprising a membrane dialyzer having inlet and outlet ports for blood and inlet and outlet ports for hepatocytes and culture medium, a semi-permeable membrane separating a first conduit for blood circulation and a second conduit for hepatocytes and culture medium circulation, a mixing vessel connected to a second conduit and has an inlet

port for introducing hepatocytes, an oxygenation means in fluid communication with the mixing vessel, a pump for circulating blood through the first conduit and a pump for circulating hepatocytes and culture medium from the mixing vessel to the second conduit (see figure 3; pages 600-602)(claims 1-2, 16, 26-27, 41). Regarding claim 7, the structural elements comprising blood circuit of Olumide et al. are inherently made of material compatible with blood. Regarding claims 8 and 32, Olumide et al. teach that hepatocytes are isolated from liver tissue of pigs (see page 599). Regarding claims 12, 14-15, 24-25, 35 and 37-38, Olumide et al. teach that curophan membrane of the membrane dialyzer are impermeable to high molecular weight proteins and partially permeable to low molecular weight proteins (see pages 605-606). Regarding claim 17, Olumide et al. teach that blood is circulated through the dialyzer at a flow rate of 150 - 250 ml/min (see page 601). Regarding claim 21, Olumide et al. teach that blood and culture medium is maintained at 37 degree Celsius via a heat exchanger (see figures 1-2; page 600). Regarding claim 42, the hepatocytes of Olumide et al. are unattached (see page 599). Claims 1-2, 7-8, 12, 14-17, 21, 24-27, 32, 35, 37-38 and 41-42 essentially differ from the apparatus and method of Olumide et al in reciting the step of incubation to allow attachment of hepatocytes to a metal containing substrate. Churchouse et al teach that rat hepatocytes are incubated to grow or maintained on a porous anodic aluminum oxide membrane support by taking advantage of number of properties such as high porosity, transparency, non-toxic, smooth surface and sterilizable (see col. 2, lines 22-37; col. 2, line 59 – col. 3, line 1; col. 3, line 52 – col. 4, line 19; col. 8, line 45 – col. 9, line 8). It would have been obvious to a person of ordinary skill in the art to provide a metal containing substrate as hepatocyte support via incubation in the apparatus and method of Olumide et al to grow or maintain hepatocytes in suspension as

suggested by Churchouse et al. Regarding claims 18-20, it would have been obvious to a person of ordinary skills in the art to adjust the flow rate of culture medium containing hepatocytes, circulation period, replenishment of hepatocytes and culture medium during circulation period to achieve optimal purification of blood.

3. Claims 3-6, 9, 11, 22-23, 30-31, 33 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olumide et al. in view of Churchouse et al. as applied to claims 1, 16, 26, 41 above, and further in view of U.S. Patent No. 5,043,260 (hereinafter referred to as Jauregui). Claims 3-4, 22-23 and 30-31 differ from the apparatus and the method of Olumide et al. in view of Churchouse et al. in reciting additional means for removal of solutes connected to the bioreactor and the mixing vessel. Jauregui teaches a method of using the apparatus for extracorporeal purification of blood and plasma comprising hollow fiber perfusion device with hepatocytes including the means for removal of solutes from hepatocytes in culture medium (62) and blood connected to the hollow fiber perfusion device (10) (see figures 1, 4, 7; col. 4, line 39 - col. 5, line 15). It would have been obvious to a person of ordinary skills in the art to modify the apparatus and the method of Olumide et al. in view of Churchouse et al. to incorporate additional means for removal of solutes connected to the bioreactor to remove waste products in culture medium and blood released by hepatocytes as suggested by Jauregui. Regarding claim 5, Jauregui teaches ultrafiltration membrane (see col. 4, lines 49-56). Regarding claim 6, it would have been obvious to a person of ordinary skills in the art to substitute hollow fiber membrane dialyzer for the membrane dialyzer of Olumide et al. for their equivalent function as dialyzers and have the lumen within the fiber as the first conduit and the exterior space of the fiber as the second conduit as suggested by Jauregui. Regarding claim 11, it would have been obvious to a

person of ordinary skills in the art to modify the apparatus of Olumide et al. in view of Churchouse et al. to use any pump to circulate biological fluid through a hollow fiber membrane such as a centripetally forced pump. Regarding claims 9 and 33, it would have been obvious to a person of ordinary skills in the art to substitute hepatocytes isolated from the liver cells of human in the apparatus of Olumide et al. in view of Churchouse et al. for hepatocytes isolated from the liver cells of pig for purification of human blood. Regarding claim 43, it would have been obvious to a person of ordinary skills in the art to use the hepatocytes attached to the membrane dialyzer for purifying blood as suggested by Jauregui (see col. 4, lines 4-34).

4. Claims 10 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olumide et al. in view of Churchouse et al. as applied to claims 1 and 27 above, and further in view of U.S. Patent No. 4,335,994 (hereinafter referred to as Gurth). It would have been obvious to a person of ordinary skills in the art to modify the apparatus of Olumide et al. in view of Churchouse et al. to use any pump to circulate biological fluid through a loop such as a boundary layer pump of Gurth.

5. Claims 13 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olumide et al. in view of Churchouse et al. as applied to claims 1 and 27 above, and further in view of U.S. Patent No. 5,011,607 (hereinafter referred to as Shinzato). It would have been obvious to a person of ordinary skill in the art to modify the apparatus of Olumide et al. to use any pump to generate a counterflow for back diffusion such as a volume changing pump device (8) of Shinzato (see abstract and figure 1).

6. Claims 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olumide et al. in view of Churchouse et al. as applied to claim 26 above, and further in view of Arnaout et

al., "Development of Bioartificial Liver:Bilirubin Conjugation in Gunn Rats", Journal of Surgical Research, April 1990, Vol. 48, No. 4, pages 379-382 (hereinafter referred to as Arnaout et al.). Claims 39-40 essentially differ from the apparatus of Olumide et al. in view of Churchouse et al. in reciting hepatocytes attached to microcarrier particles comprising collagen-coated beads. Arnaout et al. teach an apparatus for extracorporeal purification of blood and plasma comprising isolated hepatocytes attached to collagen-coated microcarriers for expression of differentiated cell function and maintaining viability of hepatocytes. It would have been obvious to a person of ordinary skills in the art to modify the apparatus of Olumide et al. in view of Churchouse et al. to substitute hepatocytes attached to collagen-coated microcarriers for prolonged viability and expressed differentiated liver cell function for more efficient removal of waste material from blood.

7. Claims 29 and 44-46 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Applicant's arguments with respect to claims 1-27 and 29-46 have been considered but are moot in view of the new ground(s) of rejection.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Kim whose telephone number is (703) 308-2350. The examiner can normally be reached on weekdays from 7:00 AM - 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Wanda Walker, can be reached on (703) 308-0457. The fax phone number for official response is (703) 892-9306.

When sending a draft amendment by fax, please mark the paper as "DRAFT"; otherwise, mark the paper "OFFICIAL". This will expedite the processing of the paper.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0651.

John Kim
Primary Examiner
Art Unit 1723

J. Kim
August 8, 2003